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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/994,468	12/19/97	LYMAN S	2813-L

HM12/0804

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EXAMINER	
KERR, J	
ART UNIT	**PAPER NUMBER**
1633	7

DATE MAILED: 08/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/994,468	Applicant(s) Lyman et al.
	Examiner Janet M. Kerr	Group Art Unit 1633

☒ Responsive to communication(s) filed on *May 20, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-8* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-8* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Arguments

Applicants' amendment, filed on 5/20/99, has been entered.

Claims 1-8 remain pending.

Claim Numbering

With regard Applicant's arguments filed 5/20/99 have been fully considered but they are not persuasive. Applicants argue that originally filed claims (claims 36 and 49) and the claims submitted in the preliminary amendment (claims 50-55) are numbered in compliance with 37 CFR 1.126).

Although the instant application is a continuation of Application Serial No. 08/444,627, a claim which is originally filed in an application, by convention, begins with the number 1. If there are several claims, they shall be numbered consecutively (see MPEP 608.01(I)). The instant application, Application Serial No. 08/994,468, is a continuing application, as indicated by Applicants, not a continued prosecution application. Thus, the numbering of the originally filed claims was incorrect. Claims 36 and 49 should be 1 and 2, respectively. Claims submitted in the preliminary amendment, i.e., claims 50-55, should be 3-8 as set forth in MPEP 608.01(j).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Lyman *et al.* (Cell, 75:1157-1167, 1993).

Lyman *et al.* disclose a stem cell expansion media comprising cell growth media, flt3-ligand, and steel factor, and a method of expanding hematopoietic cells comprising contacting the cells with flt3-ligand alone or in combination with steel factor in amounts sufficient to cause hematopoietic cell expansion (see, e.g., page 1165, under the section entitled "Hematopoiesis Assays", and pages 1161-1162, under the section entitled "Murine flt3 Ligand Stimulates the Proliferation of Human CD34-Positive Bone Marrow Cells).

Thus the method and stem cell expansion media of Lyman *et al.* anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyman *et al.* (Cell, 75:1157-1167, 1993), taken with Heimfeld *et al.* (WO 93/08268, 1993), and Hoffman *et al.* (WO92/18615, 1992).

Lyman *et al.* (Cell) disclose a stem cell expansion media comprising cell growth media, flt3-ligand, and steel factor, and a method of expanding hematopoietic cells comprising contacting the cells with flt3-ligand alone or in combination with steel factor in amounts sufficient to cause hematopoietic cell expansion (see, e.g., page 1165, under the section entitled "Hematopoiesis Assays", and pages 1161-1162, under the section entitled "Murine flt3 Ligand Stimulates the Proliferation of Human CD34-Positive Bone Marrow Cells).

The above reference does not disclose a medium formulation containing flt3-ligand and other claim-designated growth factors. However, Heimfeld *et al.* disclose a cell culture medium for expanding hematopoietic stem cells which comprises cell growth media, and growth factors such as IL-1, IL-3, IL-4, IL-6, IL-7, SF, GM-CSF, G-CSF, M-CSF, etc. (see, e.g., page 5, lines 14-29). Similarly, Hoffman *et al.* disclose a medium formulation for expanding hematopoietic stem cells comprising growth factors selected from IL-1, IL-3, IL-6, GM-CSF, GM-CSF/IL-3, as well as other growth factors (see, e.g., page 14, Table I, page 23, Table IX) As the growth factors disclosed by Heimfeld *et al.* are similarly disclosed by Hoffman *et al.*, all of which are known to stimulate expansion of hematopoietic stem cells, one of ordinary skill in the art would have had a high expectation of successfully expanding hematopoietic stem cells in a culture medium comprising flt3-ligand and an additional growth factor.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a medium formulation containing flt3-ligand and a growth factor such as SF, GM-CSF, IL-1, IL-3, G-CSF, EPO, or GM-CSF/IL-3, as formulations containing flt3-ligand in combination with other growth factors are known in the art to be suitable for expanding hematopoietic stem cells as taught by Lyman *et al.*, or by Hoffman *et al.* Moreover, it would have been obvious and well within the purview of the skilled artisan to substitute one growth factor for another, as all of the reference and claim-designated growth factors are known in the art to stimulate proliferation of hematopoietic stem cells. Thus, one of ordinary skill in the art would have had a high expectation of successfully expanding hematopoietic stem cells in a medium formulation containing flt3-ligand and other growth factors, in view of the disclosures of Lyman *et al.*, Hoffman *et al.*, and Heimfeld *et al.*, that the claim-designated growth factors stimulate hematopoietic stem cell expansion.

Thus the claimed invention as a whole was clearly *prima facie* obvious at the time the claimed invention was made especially in the absence of sufficient, clear, and convincing evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 9, and 10 of copending Application No.08/399,404. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of co-pending application Serial No. 08/399,404 are directed to a kit which comprises a cellular growth medium and a growth factor, wherein the growth factor can be selected from GM-CSF, G-CSF, IL-1, IL-3, IL-6, TPO, EPO, flt3-ligand, SF, and a GM-CSF/IL-3 fusion protein. As the composition and method of using the composition in the instant application are encompassed in the kit and the intended use of the kit, the claims are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However,

this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant is requested to return a copy of the attached Notice to Comply with the response.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Brian Stanton, Supervisory Primary Examiner of Art Unit 1633, at (703) 308-2801. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600
August 2, 1999

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1285

Application No.:08/994,468

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: the topology of the sequence was not reported.

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [ ] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE